UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/674,090	03/01/2001	Yoav Eichen	RCP-PT009	1528

3624 7590 09/19/2007

VOLPE AND KOENIG, P.C.
UNITED PLAZA, SUITE 1600
30 SOUTH 17TH STREET
PHILADELPHIA, PA 19103

EXAMINER	
KIM, YOUNG J	
ART UNIT	**PAPER NUMBER**
1637	

MAIL DATE	DELIVERY MODE
09/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/674,090	EICHEN ET AL.	
	Examiner	Art Unit	
	Young J. Kim	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-9,18-20,22-29,35-39,41,43-45,47-51 and 53-66* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *37,62,63 and 65* is/are allowed.

6)☒ Claim(s) *1,3-9,18-20,22-29,35,36,38,39,41,43-45,47-51,53-61 and 64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/9/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 9, 2007 has been entered.

Preliminary Remark

Claims 2, 10-17, 21, 30-34, 40, 42, 46, and 52 are canceled.

Claims 64-66 are new.

Claim interpretation

For the purpose of examination, the term, "target," has been assumed to be limited to biological molecules; and the term, "recognition moiety," has been also assumed to be limited to biological molecules, as when the claims are read in light of the specification, the terms are limited to the invention which pertains to biological molecules (i.e., nucleic acids, protein, antibody, etc.).

MPEP 608.01(o) states that the meaning of every term used in any of the claims should be apparent from the descriptive portion of the specification with clear disclosure as to its import.

This is necessary in order to insure certainty in construing the claims in the light of the specification, Ex parte Kotler, 1901 C.D. 62, 95 O.G. 2684 (Comm'r Pat. 1901).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 55, 56, 58, and 59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 is rejected as being indefinite for the following reasons.

Claim 3 recites that the reagents predefined in its parent claim 1 "comprise":

(i) one or more reagents to allow deposition and/or formation of said nucleation center-forming entities on a complex formed between the recognition moiety and the target; and

(ii) a combination of metal ions and a reducing agent to allow formation of said conductive substance from said entities.

The parent claim 1, however, already states that the reagents which is "formulated to deposit" conductive substance onto a complex formed between recognition moiety and the target, wherein the reagents comprise:

(i) a solution comprising nucleation center-forming entities for binding to components of said target; and

(ii) a combination of metal ions and a reducing agent to allow formation of said conductive substance on said entities.

It is unclear how the metes and bounds covered by claim 3 is different from claim 2 as it appears to be a mere rephrasing of the reagent<u>s</u> already defined in claim 1.

Claims 55, 56, 58, and 59 are indefinite for reciting the term, "means."

Their parent claim 1 has been amended to remove said term. Hence, the term, "means" appearing in claims 55, 56, 58, and 59 lack proper antecedent basis for the usage of said term.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-9, 18-20, 22-29, 35, 36, 38, 39, 41, 43-45, 47-51, 53, and 55-61 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The steps described in section [0249] through section [0251] (referencing to the patent publication of the child application 10/452,139) are critical or essential to the practice of the invention, but not included in the claim(s) is not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

The embodiment which is claimed by the instant claims are described in Figure 21, which will be reproduced below:

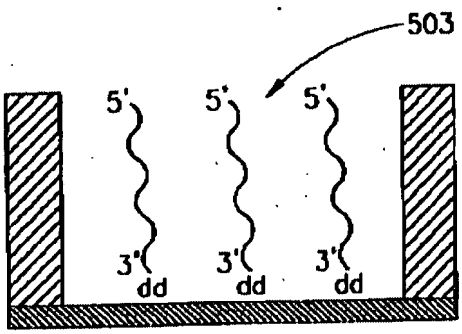


FIG.21B

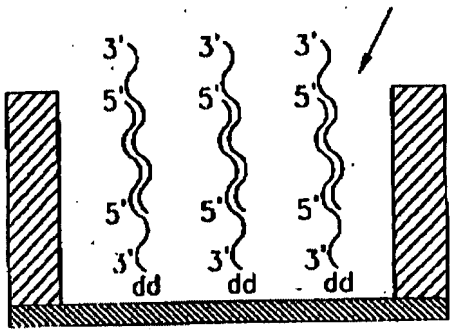
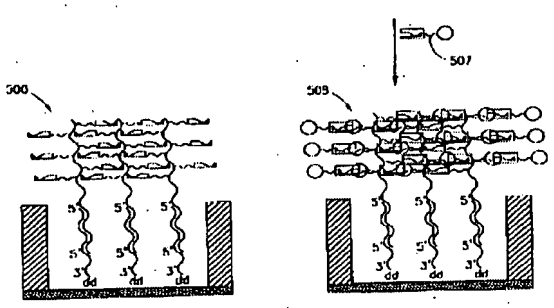


FIG.21C

The subject-claims are drawn to a device (and method of its use) depicted in Figure 21B comprises a first electrical conductor and a second electrical conductor supported by a substrate and separated by a gap, and a monolayer of oligonucleotide probes attached to the substrate in the gap between the first and second electrical conductors.

Figure 21C depicts the subsequent step of claim 1, wherein said step provides for the contacting of the recognition moieties with a sample which may or may not have the target molecule under conditions, permitting target molecules, if any, present in the sample to bind to the probes.

The subject device and its method of use is requires that a conductive coating is formed over the recognition moieties and any target molecules bound to the recognition moieties. However, for the conductive bridge to be formed, the specification is clear that a prior step of exposing the target:probe complex to a solution containing transferase and biotinylated bases which induces the elongation of the DNA skeleton at the 3'-deoxy site; **and** exposing the resulting structure to a solution containing gold colloids coupled to streptavidin units, must occur (see sections [0249] and [0250]). This is also represented by Figures 21D and 21E:



The specification is clear that upon the formation of this structure, a conductive coating over the oligonucleotide probes and any target molecules hybridized to the oligonucleotide probes can occur by contacting the structure with a solution containing hydroquinone and $Au(SCN)_2$, wherein gold deposited act as catalyst centers, allowing the colloids to ***grow and merge*** to form conductive path bridging the two gold electrodes.

Clearly, the claims do not recite the essential elements which are required to form a conductive coating over the oligonucleotide probes and the target nucleic acid molecules which would allow an electrical current to be carried between the probes, failing to enable the invention as claimed.

Claims 1, 3-9, 18-20, 22-29, 35, 36, 38, 39, 41, 43-45, 47-51, 53, and 55-61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims are drawn to the embodiment set forth in Figure 21, wherein the only discussion of said embodiment is drawn to the target molecule being nucleic acid and the recognition moieties being nucleic acids. Currently amended claims broadly embrace the target molecules and recognition moieties being nucleic acids as well as proteins and antibodies. Applicants are requested to point out specifically wherein in the specification the currently claimed embodiment is shown as being contemplated for the target molecule being protein and the recognition moiety being antibodies, wherein reagents which allow extension of a conductive bridge across the two electrodes are effected (as depicted in Figure 21).

Claim Rejections - 35 USC § 102

The rejection of claims 1, 3-5, 24-29, 35, 36, 39, 41, 43-45, 47-51, 55-57, 60, and 61 under 35 U.S.C. 102(b) as being anticipated by Braun et al. (Nature February 19, 1998, vol. 391, pages 775-778), made in Office Action mailed on March 7, 2007 is withdrawn in view of the Amendment received on July 9, 2007.

Specifically, the claims have been amended to an embodiment that is different from that which was originally claimed. The previously claimed embodiment of detection was drawn to the use of a device comprising a first and a second electrical conductor, and one or more set of oligonucleotide probes attached to the electrical conductors (as show in Figure 10), while the currently amended claims are drawn to a method of using a structurally different device, the main

notable difference being that the oligonucleotides are not immobilized to the electrical conductors, but a substrate which is formed between the two electrical conductors (as shown in Figure 21).

Braun et al. fails to disclose the use of the currently amended structure, and therefore, the rejection is withdrawn.

Claim Rejections - 35 USC § 103

The rejection of claims 6-9, 18-21, 38, 58, and 59 under 35 U.S.C. 103(a) as being unpatentable over Braun et al. (Nature February 19, 1998, vol. 391, pages 775-778), made in the Office Action mailed on March 7, 2007 is withdrawn in view of the Amendment received on July 9, 2007.

With regard to claims 6-9, 18-21, and 38, as stated previously, Braun et al. do not disclose the structure provided for by the currently amended claims nor its method of use. As the supporting references do not cure this deficiency, the rejection has been withdrawn.

With regard to claims 37, 54, 62, and 63, it as agreed that one of ordinary skill in the art would not have been motivated to arrive at the device as claimed wherein the microelectronic device comprises a plurality of layers, wherein a first group of conductors being defined as stripes in one or more first layers and a second group of conductors being defined as stripes in one or more second layers of the device, wherein each of said second layers being separated from a first layer by a non-conductive substance.

Rejection, New Grounds – Necessitated by Amendment

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the

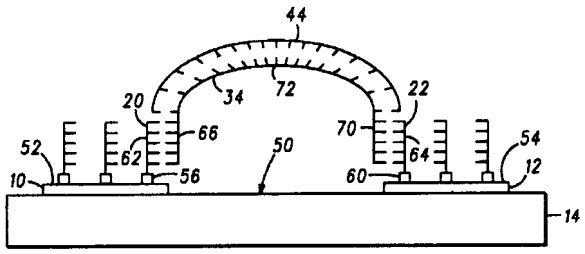
> subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 64, and 66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Braun et al. in view of in view of Maracas (U.S. Patent No. 6,060,023, issued May 9, 2000, filed March 31, 1998;) and Thorp et al. (U.S. Patent No. 5,871,918, issued February 16, 1999, filed June 20, 1996; IDS ref#AA), made in the Office Action mailed on May 19, 2006 is maintained for the reasons of record.

The teachings of Braun et al. have already been discussed above.

Braun et al. do not teach that the target nucleic acid being from bacterium, virus, or a cell, or that the recognition moiety immobilized to each of the electrodes are long oligonucleotides.

Maracas et al. disclose a method of detecting RNA (column 1, line 30; column 3, lines 12-20), employing an apparatus which comprises a first oligonucleotide and a second oligonucleotide immobilized on their respective electrodes (Figure 2; see below):



A first nucleic acid (element 34) is hybridized to these first and second oligonucleotides, thereby completing a circuit, wherein the target nucleic acid hybridizing (element 44) to said first nucleic acid results in difference in electrical conductance, allowing the detection of the target nucleic acid (column 3, lines 31-38; column 5, lines 46-67).

Thorp et al. employ their device for the method of detecting infectious agents, virus, etc. employing electrode immobilized probes which comprise sequences that are complementary to the

sequences specific to such pathogens (column 14, lines 47-51), wherein the sample being analyzed is disclosed as being blood (column 15, line 66).

It would have been *prima facie* obvious to one of ordinary skill in the art a the time the invention was made to combine the teachings of Braun et al. and the teachings of Maracas and Thorp et al., thus arriving at the claimed invention for the following reasons.

While Braun et al. are not explicit in stating that their method could be employed for a method of detecting target nucleic acid, one of ordinary skill in the art would have recognized and would have been motivated to apply the teachings of Braun et al. in view of the teachings of Maracas.

Braun et al. disclose a method of hybridizing a DNA to a pair of oligonucleotides which are separated from each other, wherein each of the oligonucleotides are immobilized on an electrode. The proper hybridization of DNA to the pair of oligonucleotides completes the circuit, thereby allowing the electricity to flow. Absent such a hybridization, the circuit would not have been completed.

Maracas discloses a concept of detecting the presence of target nucleic acids by determining the amount of conductance (i.e., flow of electricity) between two oligonucleotides which are also immobilized on an electrode.

While Maracas employs a first nucleic acid hybridized to the two oligonucleotides (thereby forming a conductive bridge), wherein the target nucleic acid is hybridized to this first nucleic acid, the concept of the detection is the same, which is based on the detection of the electricity flow.

Thus, one of ordinary skill in the art at the time the invention was made would have been clearly motivated to also apply the teachings of Maracas for the purpose of applying the method of Braun et al. in detecting a target nucleic acid (such as from virus, bacterium, or cell.) from various

samples known to contain target nucleic acids (i.e. blood; as evidenced by Thorp et al.) based on the same concept of detection based on electricity flow.

Therefore, the invention as claimed is *prima facie* obvious over the cited references.

Conclusion

Claims 37, 62, 63, and 65 are allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner is on flex-time schedule and can best be reached from 8:30 a.m. to 4:30 p.m (M-W and F). The Examiner can also be reached via e-mail to Young.Kim@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary Benzion, can be reached at (571) 272-0782.

Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent to the Official Tech Center Fax number: (571) 273-8300. For Unofficial documents, faxes can be sent directly to the Examiner at (571) 273-0785. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished

applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Young J. Kim
Primary Examiner
Art Unit 1637
9/16/2007

YOUNG J. KIM
PRIMARY EXAMINER

YJK